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14. ABSTRACT This is the third annual report submitted for this research program. The report for the first and the second aims of this project have been submitted. In the first aim, we showed significantly lower content of nucleated cells in CBUs from African/American mothers and intervention with more frequent prenatal visits did not change the cell yield. In the second aim, we demonstrated the increase access to collection of African/American CBUs through education may compensate for poor individual yield and thus prove to be an effective means of building minority CBU inventory. This final annual report is to give the report of the transplantation outcomes of African/American CBU recipients compared with other racial groups. This analysis is limited to those patients who have received an allogeneic cord blood stem cell transplantation at Karmanos Cancer Center.

15. SUBJECT TERMS
cord blood, transplantation, minority, African/American, stem cell, donor

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INTRODUCTION

The main objective of Aim 3 of this project is to determine and compare the engraftment, incidence of acute and chronic graft-versus-host disease, infectious complications and survival of African/American UCBT recipients with other racial groups. The clinical outcomes of UCBT in the minority population, especially African/American patients with various hematologic diseases, are not well studied. Search for a matched unrelated donor for African/American patients is much more difficult than the Caucasian counterpart. Therefore, cord blood transplantation is an attractive alternative for the African/American patient who is unable to find a suitable adult donor. Although many other factors also contribute to the outcome of transplantation, the greater flexibility of matching a cord blood unit to a transplant recipient allows cord blood transplantation to be a good alternative for many patients. This section will give preliminary examination of this issue.

In December 2005, President Bush signed legislation that authorized the C. W. Bill Young Stem Cell Transplantation Program as a new structure to support unrelated donor transplantation in the United States. The Program included creation of the Stem Cell Therapeutic Outcomes Database (SCTOD) to collect outcomes data for the Center for International Blood and Marrow Transplant Research (CIBMTR). Since this statistical information is undergoing reformat through the SCTOD, we will rely on the data derived from transplantation at the Karmanos Cancer Center in combination with the outcomes data obtained from the quarterly report of the National Marrow Donor Program (NMDP) functioning as the Cord Blood Coordinating Center (CBCC) for this Aim 3 annual report. Presently, the NMDP is managing the National Cord Blood Inventory (NCBI) for search and distribution of CBUs. Therefore, our center-specific data presented here is only part of the data that has been submitted to SCTOD for future analysis. The complete outcomes data will be reported by the SCTOD.

BODY

As of 12/31/07, the JP McCarthy Cord Stem Cell Bank has distributed 49 CBUs to transplant centers worldwide; three of these CBUs have not been infused. There are 8 cases with no further information available and information will not be available in the near future; these units were shipped to international sites in 6 and domestic sites in 2. Most of these units were shipped with the collaboration of the American Red Cross. There were 19 deaths among 38 patients with reported outcome data – overall a 50% survival (raw rate not Kaplan-Meier). Out of these 38 patients, there was one graft failure. It is likely that this is underestimated because of the incomplete data submission by the transplant centers. Data from these transplant sites were either captured by the European Bone Marrow Transplant Group (EBMT) or SCTOD (units distributed by NMDP). Data will be analyzed and presented by respective organizations.

At our center, we performed 28 cord blood stem cell transplantations from 1/8/99 to 12/31/07; this analysis was covered under the IRB-approved protocol D2928 (IRB approval and continuation approval is attached). These patients were candidates for allogeneic stem cell transplantation but there were no suitable adult stem cell donors identified in the donor registry. Therefore, allogeneic stem cell transplantation using cord blood was considered an option for these patients.

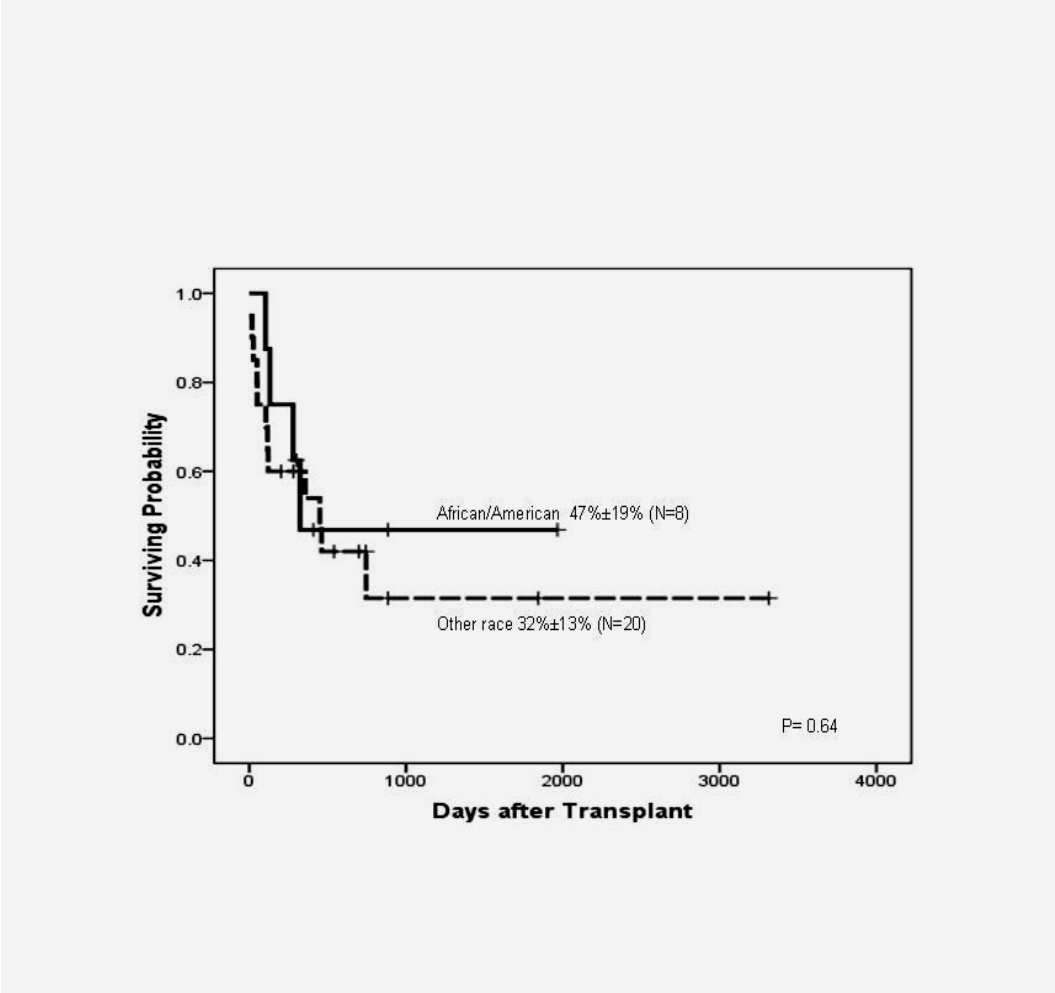
Table 1: Demographics and outcome of cord blood stem cell transplantation at the Karmanos Cancer Center

Data Category	African/American	Other	P value
Race			0.68
Male	3	11	
Female	5	9	
Median age (range)	11 (5-43)	19 (0.5-61)	
Acute GVHD	4	3	0.14
Chronic GVHD			0.22
None	7	15	
Limited	0	2	
Extensive	1	3	
Diagnosis			0.27
Aplastic anemia	2	0	
Acute lymphoid leukemia	3	5	
Acute myeloid leukemia	2	7	
Acute Biphenotypic leukemia	0	1	
Juvenile myelomonocytic leukemia	0	2	
Myelodysplastic syndrome	0	1	
Myeloma	1	0	
Non-Hodgkin lymphoma	0	2	
Osteopetrosis	0	1	
Severe combined immunodeficiency	0	1	
Preparative Regimens			0.53
Busulfan, cyclophosphamide, Ara-C	4	2	
Busulfan, cyclophosphamide	0	1	
Busulfan, cyclophosphamide, melphalan	0	2	
Busulfan, fludarabine	0	1	
Busulfan, fludarabine, TBI	1	4	
Cyclophosphamide, ATG	1	0	
Cyclophosphamide, fludarabine, TBI	0	1	
Cyclophosphamide, TBI	1	4	
Fludarabine, melphalan, TBI	1	1	
R-BEAM	0	1	
TBI, VP-16	0	2	
None*	0	1	
Causes of Death			1.0
Graft failure	0	1	
Bleeding	0	1	
Bacterial infection	1	1	
Fungal infection	0	1	
Recurrent disease	2	5	
Secondary malignancy	0	1	

* One patient did not receive conditioning regimen due to the critical clinical condition. Patient had severe combined immune deficiency on a respirator with multisystem organ failure.

There was no difference in the distribution of demographic characteristics of African/American patients and other racial groups.

Overall survivals were calculated according to the Kaplan-Meier product limit estimated from the time of transplantation to the last date of contact. The estimated 3–year survival for African/American patients was 47%±19% and for other races was 32%±13% (log rank P = 0.64). Thus, there was no significant difference of survival between African/American vs. other racial groups. No further analysis was done due to the limited number of patients.



KEY RESEARCH FINDINGS

In this small series of patients who had advanced hematologic malignancies and marrow failure states, allogeneic stem cell transplantation using cord blood stem cells can be life-saving and the survival of African/American patients is comparable to other racial groups. The strategy to improve the availability of cord blood units for minorities will need to focus on increasing accessibility of cord blood donations among African/American mothers through education and aggressive outreach programs.

REPORTABLE OUTCOMES

See KEY RESEARCH ACCOMPLISHMENT above.

CONCLUSION

Over the first year of this project, we have shown that the only maternal variable associated with total nucleated cell yield in cord blood procurement is maternal race. African/American donors had a lower nucleated cell yield and it did not appear to be correlated with the frequency of prenatal clinic visits. In concept, a lower nucleated cell count may be an inherent biologic characteristic of the African/American cord blood units. Therefore, we dedicated the second year of this project to the expansion of a campaign to increase the participation of the African/American population in cord blood donation. Through greater participation of the potential donors, we were able to increase the collection of African/American CBUs. At the same time (in the second year and continuing into the third year) we implemented a long-term strategy to involve the Wayne State University medical student as volunteers to help with the education of potential cord blood donors and to obtain informed consent for cord blood donation. We are hoping that education of future practitioners will increase the awareness of the importance of cord blood donation and will ensure continuation of cord blood procurement into the future. Lastly, in the third year, we demonstrated the practicality of cord blood stem cell transplantation in African/American patients in the absence of other donor sources. Cord blood stem cell transplantation can produce similar outcomes in African/American patients as compared to other racial groups.

The greatest benefit of funding for this project is the long-term impact on cord blood procurement and transplantation at the JP McCarthy Cord Stem Cell Bank at Karmanos Cancer Center. We are now in a position to expand cord blood collections in the community especially among African/American donors. We are also expanding our collection sites to neighboring cities as well as hospitals in Toledo, Ohio. As we increase the accessibility of the cord blood donation program, a greater number of patients will benefit from this source. Our hope is to improve the survival of patients especially among the African/American population.